NIH RELAIS Document Delivery

NIH-10105639

NIH -- W1 RA332

JANICE LEE
NIDCR/NIH, bldg 30, rm 229
Bethesda, MD 20892

ATTN:		SUBMITTED:	2002-01-08 19:22:57
PHONE:	301-435-1674	PRINTED:	2002-01-10 10:15:14
FAX:	-	REQUEST NO.:	NIH-10105639
E-MAIL:		SENT VIA:	LOAN DOC 5475342

NIH Fiche to Paper Journal

TITLE:	RADIOLOGIC CLINICS OF NORTH AMERICA
PUBLISHER/PLACE:	Saunders. Philadelphia, London,
VOLUME/ISSUE/PAGES:	1998 Nov;36(6):1241-59, xii 1241-59, xii
DATE:	1998
AUTHOR OF ARTICLE:	Wenig BM; Mafee MF; Ghosh L
TITLE OF ARTICLE:	Fibro-osseous, osseous, and cartilaginous lesions
ISSN:	0033-8389
OTHER NOS/LETTERS:	Library reports holding volume or year 0123703 9884700
SOURCE:	PubMed
CALL NUMBER:	W1 RA332
NOTES:	i do not have an ip address at this terminal.
REQUESTER INFO:	JANICELEE
DELIVERY:	E-mail: jlee@dir.nidcr.nih.gov
REPLY:	Mail:

0033–8389/98 $8.00 + .00

FIBRO-OSSEOUS, OSSEOUS, AND CARTILAGINOUS LESIONS OF THE ORBIT AND PARAORBITAL REGION

Correlative Clinicopathologic and Radiographic Features, Including the Diagnostic Role of CT and MR Imaging

Bruce M. Wenig, MD, Mahmood F. Mafee, MD, FACR, and Luna Ghosh, MD

Fibro-osseous, osseous, and cartilaginous lesions of the facial region, including the orbit and paraorbital regions (i.e., paranasal sinuses), are relatively uncommon. These lesions may share overlapping clinical, radiologic, and pathologic features causing potential difficulties in diagnosis. Included within the spectrum of orbital and paranasal sinus fibro-osseous and cartilaginous lesions are both nonneoplastic proliferation and neoplasms. The latter are further separated into benign and malignant categories. The specific entities that are discussed in this article include ossifying fibroma and its variant the psammomatoid (juvenile) active ossifying fibroma; fibrous dysplasia; osteoma; chondromyxoid fibroma; giant cell tumor (osteoclastoma); giant cell reparative granuloma; chondroma; osteoblastoma; chondroblastoma; osteosarcoma; and chondrosarcoma. This article presents the clinical, radiographic, and pathologic criteria that may assist in differentiating these lesions from one another. The value of radiographs in the histopathologic diagnosis of fibro-osseous, osseous, and cartilaginous lesions cannot be overemphasized. The histopathologic diagnosis of such a lesion should not be rendered in the absence of radiographic correlation. In contrast to similar lesions of long bones, those involving the head and neck, including orbital and paraorbital regions, often are curetted precluding comments relative to their gross appearance.

The opinions or assertions contained herein are the private view of the authors and are not to be construed as official or as reflecting the views of the Department of the Army, the Department of Defense, or the Department of the Navy.

BENIGN FIBRO-OSSEOUS LESIONS

Included under the rubric of benign fibro-osseous lesions are ossifying fibroma (and its histologic variants) and fibrous dysplasia. In the perfect world, ossifying fibroma and fibrous dysplasia would be readily differentiated on the basis of radiographic and histopathologic features. As is described later, there are both radiographic and histopathologic features that allow for separating these lesions one from the other. Craniofacial benign fibro-osseous lesions, however, may not be

From the Department of Endocrine and Otorhinolaryngic–Head and Neck Pathology, Armed Forces Institute of Pathology (BMW), Washington, DC; and the Departments of Radiology (MFM) and Pathology (LG), The Eye and Ear Infirmary (MFM), and the MR Imaging Center (MFM), The University of Illinois at Chicago, Chicago, Illinois

separable by histopathologic evaluation. Ossifying fibromas showing features normally attributable to fibrous dysplasia (e.g., lamellar bone with absent osteoblastic rimming) and fibrous dysplasia may show histologic features normally attributable to ossifying fibromas (e.g., woven bone and osteoblastic rimming). In the absence of radiographic correlation, such lesions are designated as *benign fibro-osseous lesion, not further specified.*

Ossifying Fibroma

Ossifying fibromas predilect to women and tend to occur in older age groups, most frequently seen in the third and fourth decades of life, although any age may be affected.[62] A predilection to black women has been reported.[48] Orbital and paraorbital involvement is generally asymptomatic, unassociated with pain or swelling, and is often diagnosed incidentally following radiographic examination. Symptomatic tumors manifest by displacement of teeth or as an expansile unilateral swelling that may eventually result in facial asymmetry. Ossifying fibroma has been suggested as arising from the mesenchyme of the periodontal ligament and, as such, is related to the cementifying fibroma and cemento-ossifying fibroma.[36]

Ossifying fibromas appear as tan-gray to white, gritty, and firm varying in size from 0.5 to 10 cm. Histologically, ossifying fibromas are composed of randomly distributed mature (lamellar) bone spicules rimmed by osteoblasts admixed with a fibrous stroma (Fig. 1). Although the osseous component is generally described as mature, the central portions may be woven bone with lamellar bone at the periphery. Complete bone maturation is seldom seen. A fibrous stroma may be densely cellular; mitotic figures are rare to absent. Secondary changes, including hemorrhage, inflammation, and giant cells, may be seen. The differential diagnosis of ossifying fibroma is primarily with fibrous dysplasia (see later). For ossifying fibromas, surgical excision is the treatment of choice and the well-circumscribed nature of this lesion allows for relatively easy removal. The prognosis is excellent following complete excision. Recurrences rarely occur.

Radiologic features depend on the stage of development and amount of mineralized matrix present. A lesion is seen as a well-circumscribed or sharply demarcated mass with smooth contours (Fig. 2). In its early stage, the lesion may appear as a solitary cystlike or solid soft tissue with minimal or no mineralized (calcified) components. At a later stage, the lesions become radio-opaque. On CT scans, ossifying fibromas appear as a expansile mass, surrounded by a thick or thin radiodense rimming. There may be islands of bone formation within the lesion (see Fig. 2). On MR imaging scans, ossifying fibromas appear heterogeneous and usually show intermediate signal on T1-weighted and hypointense signal on T2-weighted MR images. There is moderate contrast enhancement on postgadolinium pentetic acid (Gd-DTPA) T1-weighted MR imaging scans.

Variants of Ossifying Fibroma

Included within the spectrum of ossifying fibroma are its variants, which are essentially the same lesion but perhaps differ in either the nature of the calcified material that is present (cementum versus bone); in the location of the lesion in question (oral versus paranasal sinus or orbital); or in other morphologic variations (presence of psam-

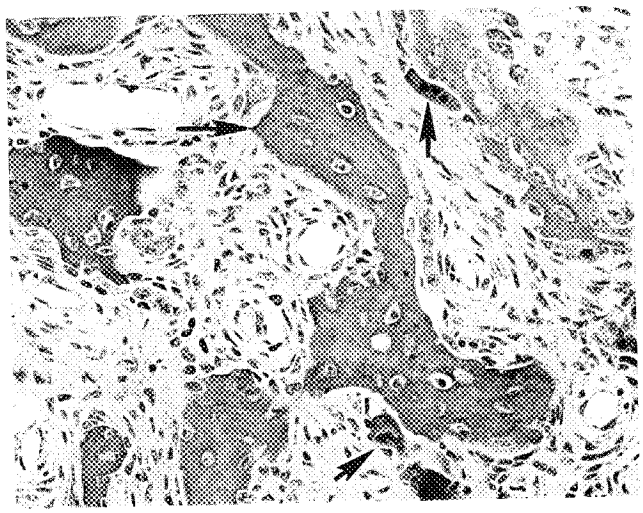

Figure 1. Ossifying fibroma. This fibro-osseous lesion is characterized by the presence of mature (lamellar) bone *(large arrow)*, rimmed by osteoblasts *(small arrows)*, and mixed with a fibrous stroma.

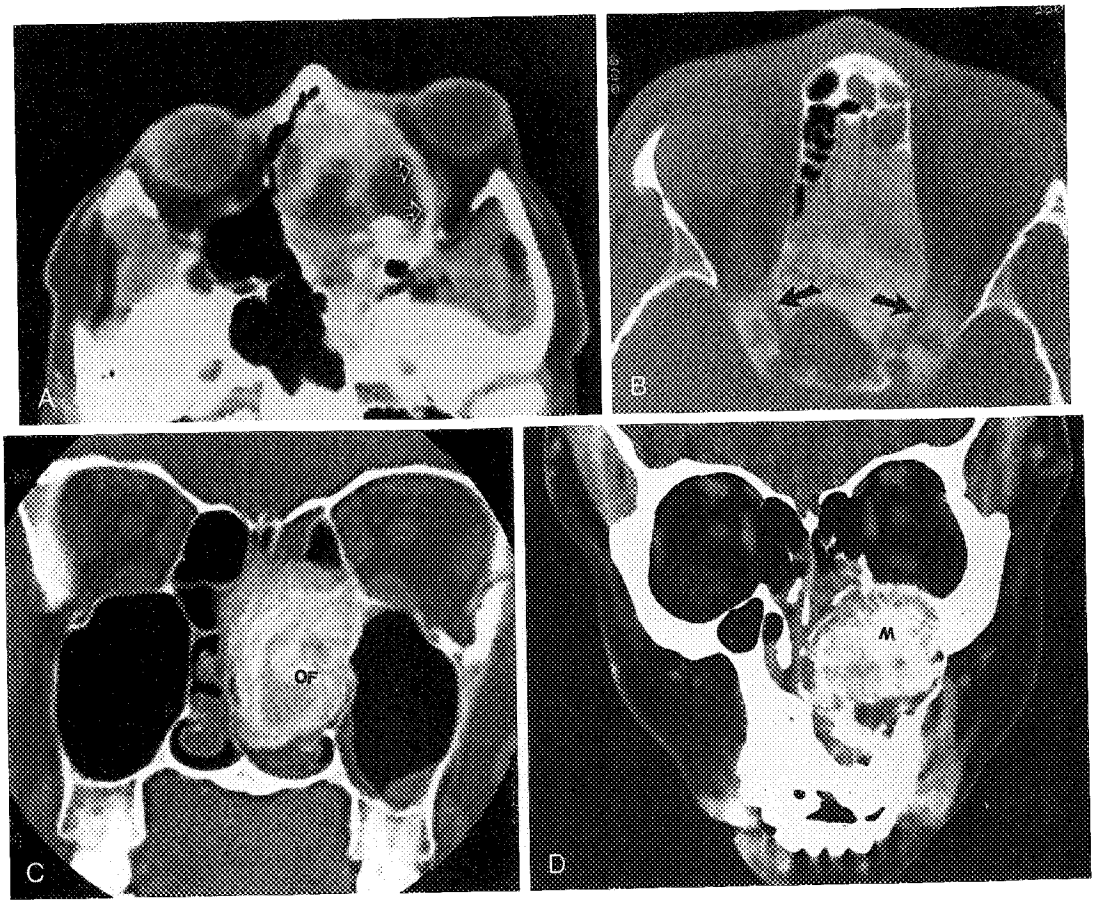

Figure 2. *A*, CT scan shows an ossifying fibroma. Note moderately thick peripheral sclerotic rim *(arrows). B*, CT scan in another patient shows typical CT appearance of fibrous dysplasia. Note constriction of both optic nerve canals *(arrows). C*, CT scan shows an ossifying fibroma (OF). (Courtesy of M. Friedman, MD.) *D*, CT scan shows expansile mineralized mass (M) involving left maxillary antrum as well as alveolar process of maxilla. This 36-year-old woman presented with a 5-month history of minor facial pain and nasal stuffiness. Pathologic diagnosis was fibrous dysplasia. As seen on CT, the lesion behaves as mass and as such, the diagnosis is characteristic of ossifying fibroma.

momatoid concretions) and overall biologic behavior (aggressive versus static). Gnathic lesions likely originate from periodontal ligament origin. The cells of the peridontal ligament are capable of producing cementum, bone, or fibrous tissue.[22] Such lesions, depending on the presence of cementum or bone, are designated as *cementifying fibromas or ossifying fibromas*. Those lesions with an admixture of both matrix material are called *cemento-ossifying fibromas*. The histogenesis for similar-appearing lesions that occur in areas not associated with the periodontal ligament (e.g., paranasal sinuses, orbit) is not entirely known. It is possible that these lesions originate from displaced periodontal ligamentous tissue in embryogenesis. Alternatively, they originate from other cells capable of producing cementum, bone, and fibrous tissue. In the orbital and paraorbital regions, these lesions usually lack cementum; may have oval-to-round calcified concretions with concentric laminations (psammomatoid concretions); and may behave in a locally aggressive manner with extension into adjacent anatomic compartments and destruction of bony confines. These lesions have been designated under a variety of names, including aggressive psammomatoid ossifying fibromas[65] and juvenile active ossifying fibroma.[36]

Psammomatoid Active Ossifying Fibroma

The psammomatoid active ossifying fibroma, also called the *aggressive psammomatoid ossifying fibroma*, is a variant of conventional ossifying fibroma that typically occurs in the sinonasal tract and potentially may behave aggressively with locally invasive and destructive capabilities.[65] There is no gender predilection. These lesions occur in younger age groups (first and second decades) resulting in their designation as juvenile psammomatoid ossifying fibroma. Their designation as juvenile, however, is not always accurate because they occur over a wide age range, including older-

aged individuals.[65] Presenting symptoms include facial swelling, nasal obstruction, pain, sinusitis, headache, and proptosis. These lesions may occur in any area of the sinonasal tract but tend to predilect to the ethmoid sinus and supraorbital frontal region.[36, 65] There may be involvement of a single site or multiple sinuses, and the orbit may be involved.

The radiologic appearance is that of a lytic or mixed lytic–radiopaque osseous or soft tissue mass varying from well-demarcated to invasive with bone erosion. The histology is that of a benign fibro-osseous proliferation composed of bony spicules and spherules admixed with a fibrous stroma. The most distinctive component is the presence of mineralized or calcified psammomatoid bodies or ossicles (Fig. 3). These ossicles vary from a few in number to a dense population of innumerable spherical bodies. The ossicles are demarcated with a central blue-to-black appearance surrounded by a pink-appearing rim and with concentric laminations. The ossicles vary from small with a round-to-oval shape to a larger irregularly shaped ossicle patter, and are present within the bony trabecules as well as within the adjacent cellular stroma. Osteoclasts are present within the ossicles and osteoblasts can be seen along their peripheral aspects. The bony trabecules vary in appearance and include odd shapes with a curvilinear pattern to coarse bone trabeculae. The trabecules are composed of lamellar bone with associated osteoclasts and osteoblastic rimming. Transition zones between the spherical ossicles and bony trabeculae can be seen. The nonosseous component includes a cellular stroma with a fascicular-to-storiform growth composed of round-to-polyhedral spindle-shaped cells with prominent basophilic nuclei and apparent cytoplasmic borders. Mitotic figures can be seen but mitotic activity is not prominent and atypical mitoses are not present. Cellular pleomorphism may be present but anaplasia and necrosis are not identified. Giant cells can be seen among the psammomatoid ossicles or scattered throughout the nonosseous stromal component. Osteoid formation may be focally present.

Complete surgical excision is the treatment of choice. The prognosis is good following complete excision but recurrences may occur and the tumors may behave in an aggressive manner with local destruction and potential invasion into vital structures.[65]

Radiologic features are similar to ossifying fibroma with admixture of both soft tissue and bone density pattern. The lesion has an aggressive appearance with marked expansion of bone with apparent cortical break. Periosteal reaction and new bone formation, seen in osteochondrogenic sarcomas, is not a feature of ossifying fibroma or psammomatoid active ossifying fibroma. The lesion may extend into surrounding tissue by virtue of expansion but not invasion (Fig. 4). On CT and MR images there may be areas of soft tissue fluidlike level. The most characteristic feature is the presence of numerous round or oval calcified bodies of varied sizes, representing the psammotoid (cementicle) bodies (see Fig. 4). The MR imaging appearance of psammomatoid active ossifying fibroma is also similar to ossifying fibroma. On T2-weighted images there may be areas of hyperintensity signal simulating cysts or soft tissue fluid levels.

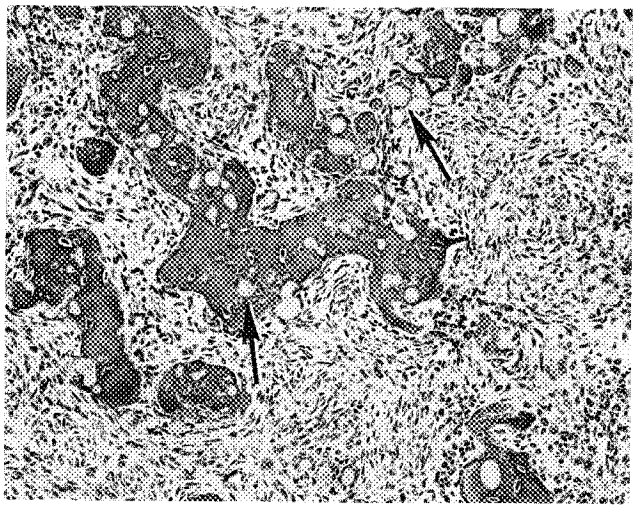

Figure 3. Aggressive psammomatoid ossifying fibroma. The most distinctive component of this variant of ossifying fibroma is the mineralized or calcified psammomatoid bodies or ossicles. The ossicles vary from small, with a round to oval shape, to a larger, irregularly-shaped ossicle pattern, and are present within the bony trabecules as well as within the adjacent cellular stroma *(arrows)*.

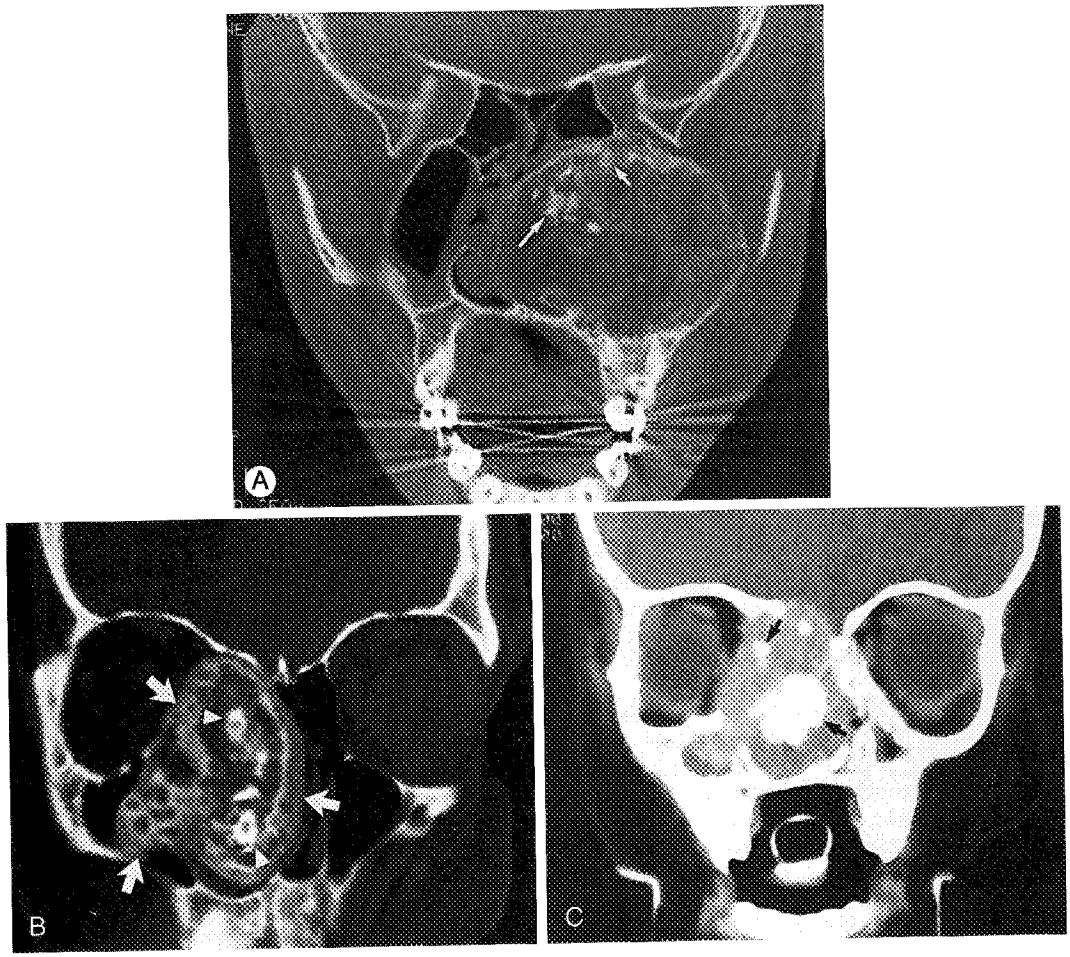

Figure 4. Aggressive psammomatoid ossifying fibroma. *A*, CT scan shows a large expansile mass of mixed intensity. Note psammomatoid bodies *(arrows)*. *B*, CT scan in another patient shows an ossifying fibroma *(arrows)*. The lesion is less aggressive than the lesion shown in *A*. Note CT appearance of psammomatoid bodies *(arrowheads)*. *C*, CT scan in a 18-month-old child shows a soft tissue mass, with involvement of medial wall of the orbit as well as the roof of the ethmoid bone. Note intralesional islands of calcifications *(arrows)*. Pathologic diagnosis was felt to be most consistent with aggressive fibro-osseous lesion (fibrous dysplasia versus ossifying fibroma). (Courtesy of Tony Peduto, MD, Westmead, Australia.)

Fibrous Dysplasia

Fibrous dysplasia is an idiopathic bone disease in which normal medullary bone is replaced by structurally weak fibrous and osseous tissue. Whether fibrous dysplasia is a nonneoplastic or neoplastic lesion remains the subject of debate. Fibrous dysplasia may be monostotic (only a single osseous site is involved) or polyostotic (involvement of two or more bones). The majority of patients affected by fibrous dysplasia are under 30 years of age and usually are in the first two decades of life. Craniofacial symptoms of fibrous dysplasia include painless, asymmetric swelling associated with functional disturbances. In the orbital and paraorbital regions, signs and symptoms may include headaches, proptosis, and nasal obstruction. Involvement of the craniofacial or jaw regions occurs in up to 50% of patients with polyostotic lesions and up to 25% in patients with monostotic lesions.[24, 27] There are no known etiologic factors. A small percentage of fibrous dysplasia occurs in Albright-McCune-Sternberg syndrome characterized by the triad of polyostotic fibrous dysplasia; endocrine dysfunction (hyperthyroidism or sexual precocity, the latter predominantly identified in girls); and cutaneous hyperpigmentation.[1, 45] Congenital fibrous dysplasia, also known as *cherubism*, is an autosomal dominant disease characterized by bilateral swelling of gnathic bones, usually the mandible.[2] Expansion of the maxilla with involvement of the maxillary sinuses and infraorbital ridge of the maxilla produces upward bulging of the orbital floor resulting

in lifting of the eye, exposure of the lower portion of the sclera, and tightening of the overlying facial skin with retraction of the lower eyelids.[10] The overall result is the cherubic appearance as depicted in Renaissance art with looking upward toward heaven.

Histologically, the fibrous tissue component is nondescript without pattern and is of variable cellularity. The osseous component includes irregularly shaped trabeculae of osteoid and immature (woven) bone arising metaplastically from the fibrous stroma; is poorly oriented with misshapen bony trabeculae, increased cellularity, and irregular margins; and forms odd geometric patterns including "C"- or "S"-shaped configurations (so-called *Chinese characters*) (Fig. 5). The trabeculae typically lack osteoblastic rimming. Multinucleated giant cells, macrophages, increased vascularity, and calcification may be seen. Under polarized light bone appears woven rather than lamellar; however, lamellar bone can be seen in fibrous dysplasia and its presence does not exclude the diagnosis. Infiltration of surrounding tissues, including normal bone, correlates with the poorly defined lesion seen by radiographic studies.

Fibrous dysplasia and ossifying fibromas may be histologically indistinguishable. Therefore, the diagnosis and differentiation rests on the clinical-radiologic-histopathologic correlation. The differentiation of ossifying fibromas from fibrous dysplasia is important because the therapeutic rationale differs for these lesions. For fibrous dysplasia, conservative surgical excision is the preferred treatment and is indicated only in cases with compromise of function, progression of deformity, pain, associated pathologic fracture(s), or the development of a malignancy. The disease may stabilize at puberty, and in children therapy should be delayed if possible until after puberty.[29] Recurrence rates are low and death due to extension into vital structures rarely occurs. Radiation treatment is not utilized because of the risk of inducing malignant transformation.[20]

Diagnostic Imaging

The radiologic features of fibrous dysplasia depend on the stage of development and amount of bony matrix within the lesion. Radiographic changes range from lucent zones to diffuse areas of sclerosis (Fig. 6). Periosteal reaction is not a feature of benign fibro-osseous lesions. Facial bones and base of the skull are preferentially involved by the sclerotic form of fibrous dysplasia. Lytic form is often seen in cranial bones. Expansion of involved bone with a heterogeneous pattern of CT densities, along with intact thin cortex, is characteristic of fibrous dysplasia. In ossifying fibroma, often there is a moderately thick peripheral rim of bone density present (see Fig. 4). Fibrous dysplasia has an intermediate signal on T1-weighted and heterogeneous hypointense signal on T2-weighted MR images. There may be areas of T2 hyperintensity, particularly in early stages of the disease. Following intravenous administration of Gd-DTPA, there is often moderate to marked contrast enhancement. Fibrous dysplasia or ossi-

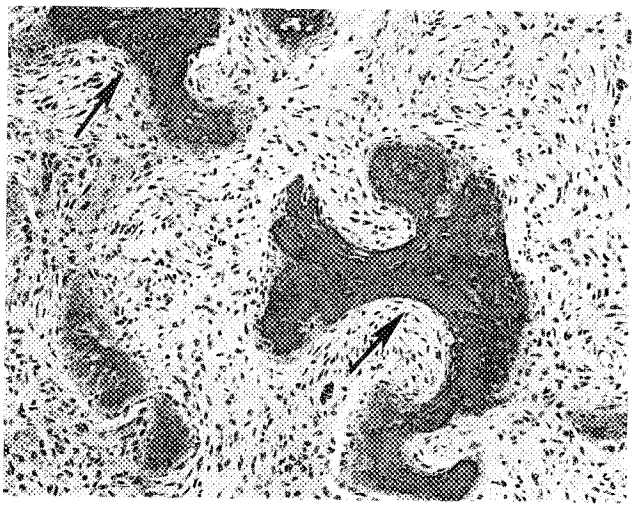

Figure 5. Fibrous dysplasia. In contrast to ossifying fibromas, the osseous component of fibrous dysplasia includes irregularly shaped, immature (woven) bone that typically lacks osteoblastic rimming *(arrows)*. The fibrous tissue component is similar to that of ossifying fibroma and includes nondescript, fibrous tissue without pattern and is of variable cellularity.

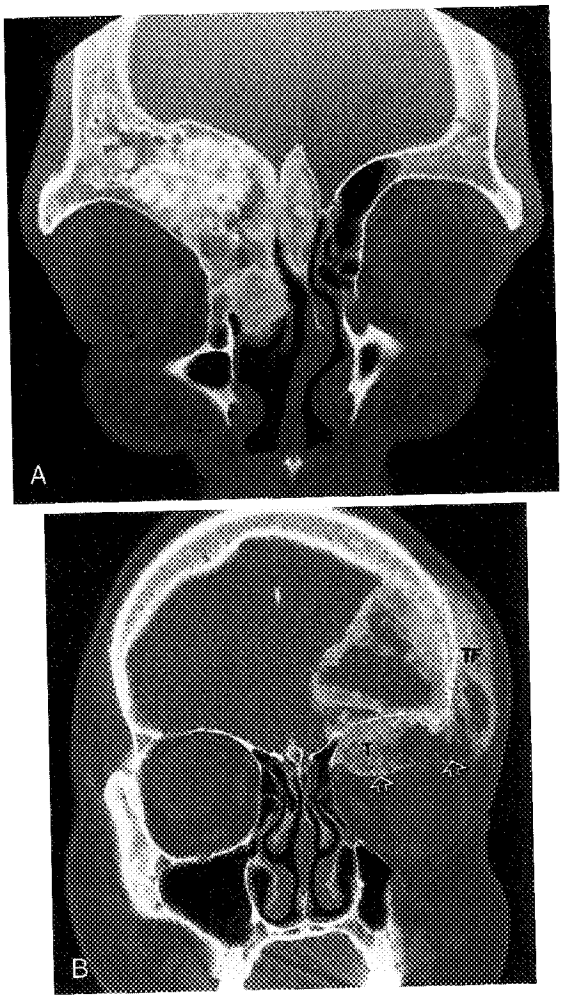

Figure 6. Fibrous dysplasia. *A*, CT scan shows characteristic changes with bone expansion compatible with fibrous dysplasia. Note lack of periosteal elevation. *B*, CT scan in a patient with osteogenic sarcoma shows mixed osteoblastic-osteolytic pattern. Note subperiosteal tumor bone formation (T) and displaced periosteum *(arrows)*, which are characteristic of osteochondrogenic sarcomas. Note invasion of temporal fossa (TF) with intratumoral bone formation.

fying fibroma may be mistaken for meningioma on MR imaging scans (Fig. 7).

OSTEOMA

Osteomas are benign bone-forming tumors that are almost exclusively identified in the craniofacial skeleton. In the craniofacial region, osteomas may be found in all sites but are most common in the frontal and ethmoid sinuses.[15, 20] These tumors are usually asymptomatic and are found by radiographic studies. Symptoms associated with paraorbital osteomas include headaches, facial swelling or deformity, and ocular disturbances.[3] Paraorbital osteomas are more common in men and occur over a wide age range but are most often encountered in the second to fourth decades of life. Paraorbital osteomas usually occur as a single lesion but may be associated with Gardner's syndrome, an inherited autosomal dominant trait characterized by intestinal (colorectal) polyposis; soft tissue lesions (fibromatosis, cutaneous epidermoid cysts, lipomas, leiomyomas); and multiple craniofacial osteomas.[8] Histologically, osteomas are well-circumscribed, composed of dense, mature, predominantly lamellar bone sometimes rimmed by osteoblasts (Fig. 8). Interosseous spaces may be composed of fibrous, fibrovascular, or fatty tissue, and hematopoietic elements may be present. Osteomas require no treatment but surgical excision may be required for symptomatic osteomas or for cosmetic reasons. Complete surgical excision is curative.

Diagnostic Imaging

The radiographic appearance is that of a sharply delineated radiopaque lesion arising and confined to bone or protruding into a sinus. At times the border may be irregular (Fig. 9).

GIANT CELL TUMOR (OSTEOCLASTOMA)

Giant cell tumors are benign but locally aggressive neoplasms characterized by the presence of osteoclast-like giant cells admixed with epithelioid and spindle-shaped mononuclear cells. Giant cell tumors are also refered to as *osteoclastoma* due to the resemblance of the giant cells to osteoclasts. Giant cell tumors of the head and neck are uncommon.[6, 54, 57] The most common sites of occurrence include the sphenoid, temporal, and ethmoid bones. Symptoms include headache, diplopia, decreased vision, and proptosis.[16] Multicentric tumors are uncommon, but when present may be associated with a more aggressive clinical course.[13]

Histologically, giant cell tumors are characterized by the presence of multinucleated giant cells and mononuclear cells. The giant cells are evenly distributed throughout the lesion and include the presence of numerous nuclei that tend to cluster in more central portions of the cell (Fig. 10). The number of nuclei in any giant cell varies and may sometimes number a hundred or more. The stromal mononuclear cells may appear epithelioid or spindle-shaped and share similar nuclear features with those seen in the giant cells. There may be increased mitotic figures in association with the stromal mononuclear cells but not in the multinucleated giant cells. The multinucleated giant cells are felt to originate from fusion of the mononuclear cells.[58] Giant cell tumors lack matrix production but in the presence of a pathologic fracture, osteoid (reactive new bone) may be present. The

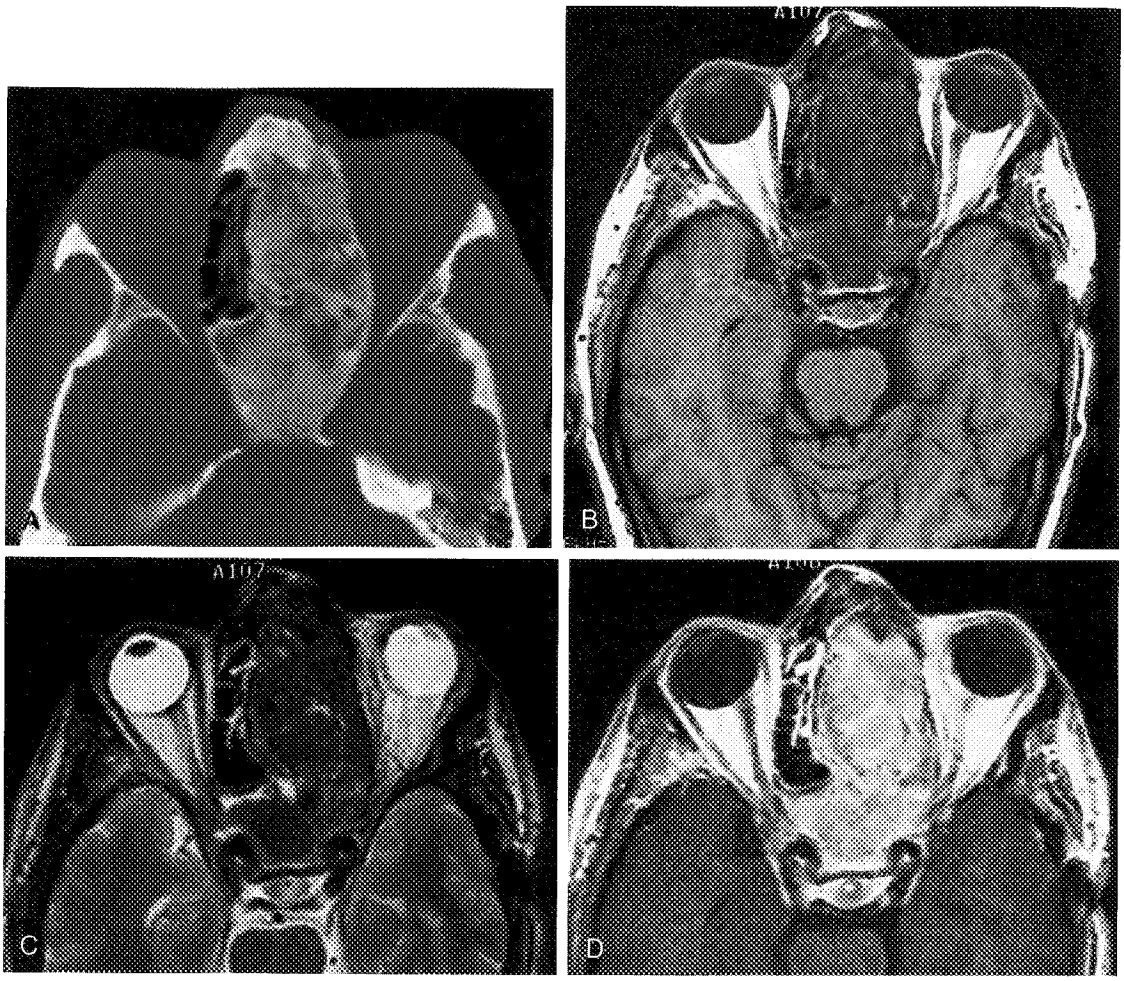

Figure 7. Fibrous dysplasia CT scan *(A)*, T1-weighted MR image *(B)*, T2-weighted MR image *(C)*, and enhanced T1-weighted MR image *(D)*, showing typical CT and MR appearance of fibrous dysplasia. The lesion is hypointense on T1-weighted and markedly hypointense on T2-weighted MR images and shows marked enhancement on post Gd-DTPA MR scan (D). Note that enhancement is more pronounced in areas that are less mineralized.

presence of chondroid matrix is unusual and, if present, likely represents evidence that the lesion in question is not a giant cell tumor. In addition, thin-walled vascular spaces, hemorrhage, and hemosiderin-laden macrophages (foam cells) can be seen. Intravascular invasion by the giant cells can be seen but is not considered a feature that is associated with more aggressive behavior. Intralesional collagen is usually absent or is focally present. Increased collagen may be present due to trauma as might occur following pathologic fracture or prior biopsy.

Diagnostic Imaging

The CT appearance of a giant cell tumor of sphenoid sinus is shown in Figure 11. The MR imaging characteristic of an ethmoid giant cell tumor is shown in Figure 12. Enhanced T1-weighted MR images are most valuable in detecting recurrent tumor (see Fig. 11C). The treatment for giant cell tumors is surgical excision, with the extent of surgery dependent on the size and extent of the tumor. Up to 60% of giant cell tumors recur if treated by simple curettage alone.[18] Cryosurgery has also been utilized as an alternative treatment modality and has been shown to be an effective treatment option.[41] Radiotherapy has been used in the treatment of giant cell tumors but is usually reserved for lesions that are not amenable to surgical resection and cryotherapy. Although the older literature indicates that giant cell tumors were radioresistant and prone to malignant transformation following radiotherapy, more current findings utilizing supervoltage radiation indicate that giant cell tumors are radioresponsive and not subject to increased incidence of sarcomatous transformation following radiation.[28, 55]

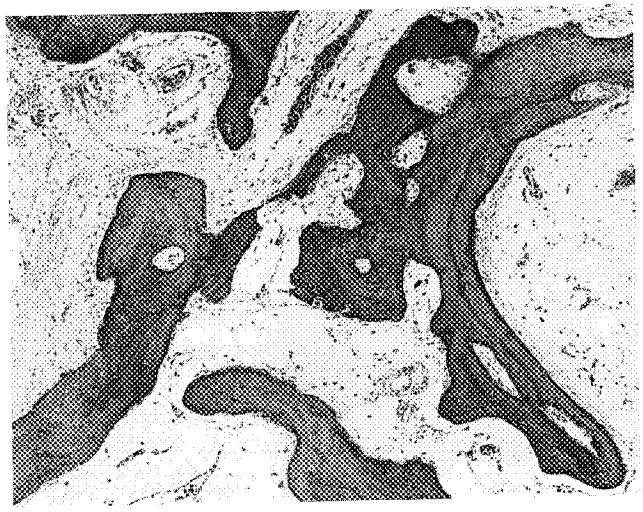

Figure 8. Osteomas are composed of dense, mature, predominantly lamellar bone. The interosseous spaces include fibrous, fibrovascular, and fatty tissue.

GIANT CELL REPARATIVE GRANULOMA

Giant cell reparative granuloma is a benign reactive osseous proliferation. Giant cell reparative granulomas share many features with aneurysmal bone cysts and in many regard these lesions may be indistinguishable.[49] In the head and neck area, the maxilla and mandible are the most common sites of occurrence. Orbital, paraorbital, or nasopharyngeal involvement is less common. Those lesions that are predominantly confined to intraosseous sites (e.g., jaws) are referred to as *central giant cell reparative granulomas* and those primarily involving soft tissues (e.g., paraorbital, sinonasal or oral) are termed *peripheral giant cell reparative granulomas*.[30, 57] Paraorbital involvement is associated with pain and swelling. Head and neck giant cell reparative granulomas are more common in women and occur in patients under 30 years of age (most are less than 20 years old).[63] Hormonal factors may influence the growth of giant cell reparative granulomas.[40, 46]

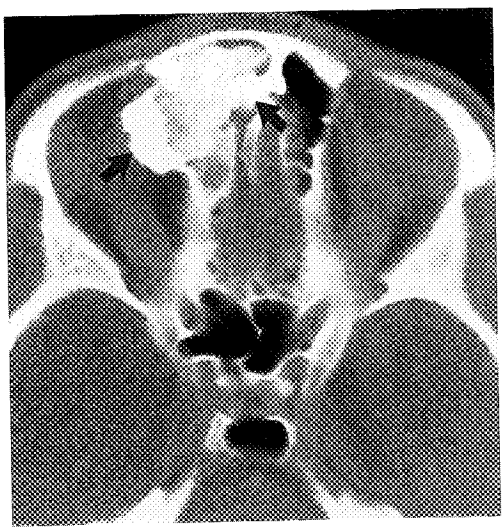

Figure 9. CT scan shows an ivory osteoma *(arrows)*.

The central and peripheral giant cell reparative granulomas are histologically identical, composed of a cellular fibroblastic stroma that includes multinucleated giant cells (Fig. 13). The giant cells are unevenly distributed but tend to be clustered in limited areas of the lesion. The giant cells often aggregate in and around foci of hemorrhage or are seen in vascular spaces. Less often, the giant cells are diffusely distributed in the fibroblastic stroma. The giant cells are smaller with fewer nuclei than those seen in giant cell tumor. The stroma includes spindle-shaped to oval-appearing fibroblasts. Mitotic figures are seen in the fibroblasts but not the giant cells; in general, the mitotic activity is less as compared with giant cell tumors. Both the giant cells and stromal fibroblasts lack cytologic atypia. Cyst formation and reactive bone may be present. The latter may or may not include osteoblastic rimming. A stromal inflammatory cell infiltrate, including lymphocytes and plasma cells, is present.

Other than giant cell tumor (see previous), the differential diagnosis of giant cell reparative granuloma includes the brown tumor of hyperparathyroidism. In fact, the histology of these two lesions is identical.[47] As such, all patients suspected of having a giant cell reparative granuloma should be evaluated for hyperparathyroidism with laboratory determination of serum calcium, parathyroid hormone, phosphate, and alkaline phosphase levels.

Surgical curettage is the treatment of choice. Up to 15% of gnathic lesions recur,[63] but sinonasal tract lesions are less likely to recur following curettage.

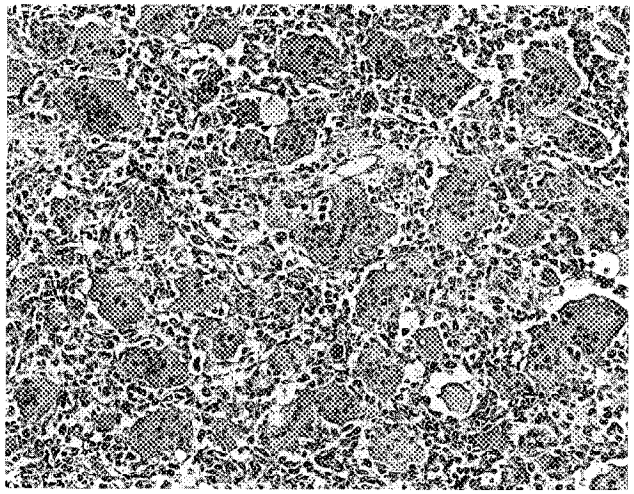

Figure 10. Giant cell tumor characterized by the presence of multinucleated giant cells and mononuclear cells. The giant cells are distributed evenly throughout the lesion and include the presence of numerous nuclei that tend to cluster in more central portions of the cell. The stromal mononuclear cells appear epithelioid and spindle-shaped.

OSTEOBLASTOMA

Osteoblastoma is a benign osteoblastic neoplasm sharing histologic appearance with osteoid osteoma but of larger size. Osteoblastomas are uncommon osseous neoplasms accounting for about 3% of all benign osseous neoplasms.[13] Osteoblastomas occur in the vertebrae; long bones, particularly the femur and tibia; and in small bones of the hands and feet. Head and neck sites of involvement include the mandible (most common site); maxilla; temporal bone; orbit; and paranasal sinuses. Osteoblastomas occur more often in men and although these tumors can occur at any age, the majority of patients (70% to 90%) are under 30 years of age.[25, 44] Signs and symptoms associated with head and neck involvement include pain, facial swelling and asymmetry, loosening of teeth, and eating problems. In contrast with osteoid osteoma, the pain associated with osteoblastoma is less often nocturnal and less responsive to aspirin. There are no known causative factors.

Histologically, osteoblastomas are hypercellular with haphazardly arranged interlacing trabeculae of osteoid associated with a loose fibrovascular connective tissue (Fig. 14). The osseous trabeculae are composed of woven bone, vary in thickness, and are lined by uniform-appearing osteoblasts. The osteoid may appear lacelike as seen in osteosarcoma but cartilaginous differentiation is not seen. The osteoblasts are plump with enlarged, hyperchromatic nuclei and increased mitotic activity. The latter include typical mitotic figures but, in contrast with osteosarcoma, atypical mitoses are not present. Further, neither nuclear pleomorphism nor an anaplasia are present. Multinucleated giant cells are variably present and in any given lesion may be prominently seen. The cellular component in osteoblastoma appears loose with intervening fibrovascular stroma. The stroma contains prominent dilated capillaries, extravasated blood, and fibrous tissue.

Diagnostic Imaging

On CT scans, osteoblastoma appear as a well-defined round expansile lesion with prominent calcified rim. The central portion may have a similar appearance as ossifying fibroma (see Fig. 15). On MR imaging, osteoblastomas appear to have similar MR imaging characteristics to ossifying fibroma. The central portion may be hyperintense on T2-weighted MR images. Osteoblastoma may show moderate to marked enhancement on Gd-DTPA–enhanced T1-weighted images.

Conservative surgery, including curettage or local excision, is the treatment of choice and is curative. Incompletely excised lesions may recur, although partially resected or incompletely curetted tumor may regress.[44] Radiotherapy may be used for those tumors that cannot be surgically removed or for recurrent tumor. Rarely, postradiation sarcomas have been reported.[44]

OSTEOSARCOMA (OSTEOGENIC SARCOMA)

Up to about 10% of conventional osteosarcomas occur in the head and neck region.[4, 13, 61] Craniofacial osteosarcomas (excluding those arising in the

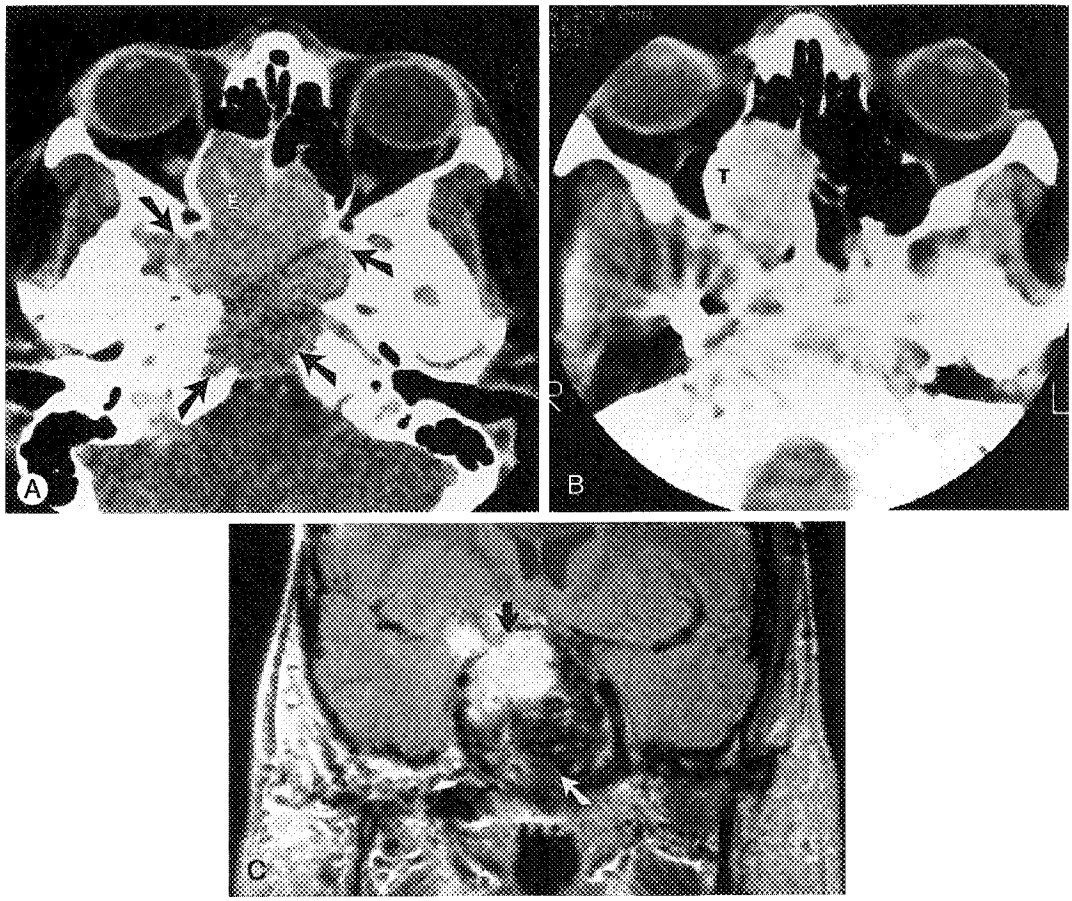

Figure 11. Giant cell tumor. *A*, Contrast-enhanced CT scan shows a destructive lesion *(arrows)* involving sphenoid sinus, including the clivus, and invading the posterior ethmoid air cells (E). *B*, Contrast-enhanced CT scan shows recurrence of tumor (T). *C*, Enhanced coronal T1-weighted MR image. Note enhancement of recurrent tumor *(black arrow)*. Note the bone chips placed inside the sphenoid sinus at time of surgery *(white arrow)*.

setting of Paget's disease) have an equal gender predilection and occur in patients who are generally a decade or two older than those with extrafacial osteosarcomas.[42, 61] The jaws are most commonly affected, with the mandible more often involved than maxilla.[4, 13, 61] Osteosarcomas may occur in other head and neck sites, including the paranasal sinuses, orbital region, and the skull.[42] The most common clinical complaints include painful swelling of the face, dentition problems, nasal obstruction, and epistaxis. Elevated serum alkaline phosphatase represents the sole laboratory value of clinical import in osteosarcoma and an abrupt elevation in patients with pre-existing benign bone lesions may be indicative of malignant transformation.

Most osteosarcomas occur de novo without an identifiable pre-existing condition. Osteosarcomas may develop secondary to a pre-existing bone disease, however, including Paget's disease, fibrous dysplasia, osteoblastoma, osteochondromas, giant cell tumors, chronic osteomyelitis, osteogenesis imperfecta, and bone infarct.[60] Ionizing irradiation is also implicated in the development of osteosarcoma.[13, 34, 42] Osteogenic sarcoma may be familial.[26] Patients with the heritable form of retinoblastoma are at risk (approximately 10% by age 25 years) of developing osteosarcoma.[14] Retinoblastoma and osteosarcoma share a deletion in chromosome 13 resulting in inactivation of the antioncogene, retinoblastoma gene.[5]

The gross appearance of osteosarcoma is dependent on the extent of mineralization versus the extent of the stromal component. As such, osteosarcomas vary from firm, hard, and gritty to fleshy and fibrous. The histopathologic features of osteosarcoma include a sarcomatous stroma intimately admixed and giving rise to osteoid (Fig. 16). Osteoid, the unmineralized precursor of bone, appears as eosinophilic, hyalinlike material with irregular contours, and is surrounded by a rim of osteoblasts. Stromal cells display variable anaplasia and are spindled to polygonal composed of hyperchromatic nuclei with or without nucleoli. Tumor giant

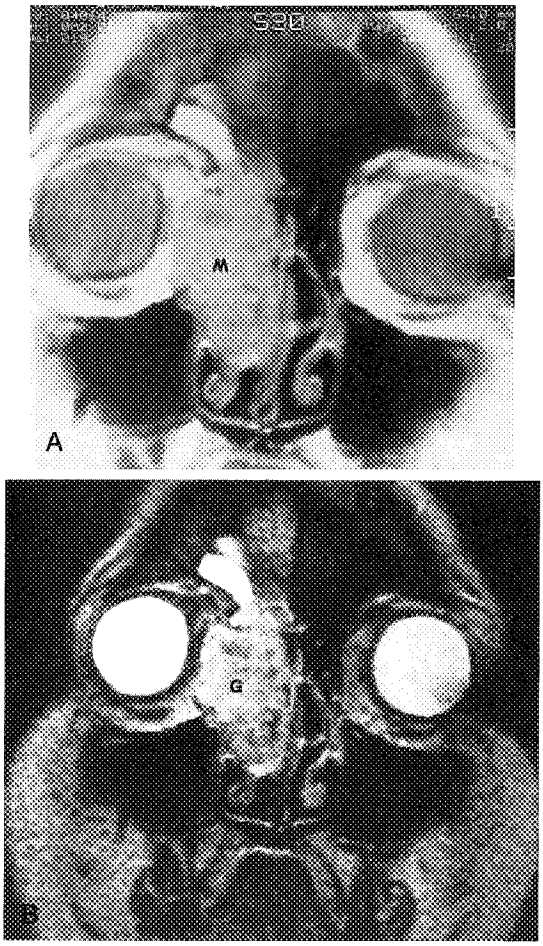

Figure 12. Giant cell tumor. *A*, Proton-weighted MR scan shows a soft tissue mass (M) involving right ethmoid and nasal cavity, invading the orbit, and compatible with the giant cell tumor. *B*, T2-weighted MR scan. The giant cell tumor (G) appears hyperintense.

cells are often seen and benign osteoclastlike multinucleated giant cells are identified in approximately 25% of cases. Necrosis, invasive growth, and mitotic activity, including typical and atypical (bizarre) mitoses, are commonly present. Tumor vascularity varies from relatively inconspicuous to dominant. The histologic grading of osteosarcomas is based on the relative anaplasia of the stromal component. Low-grade (grade I) tumors are the best differentiated and least anaplastic, whereas high-grade (grade IV) tumors are the least differentiated and most anaplastic. Osteoblasts are multipotential cells capable of producing chondroblastic and fibroblastic foci, and depending on which component predominates, osteosarcomas are divided into osteoblastic, chondroblastic, and fibroblastic types. The prognosis in osteosarcoma, however, does not correlate with the histologic subdivision.[17, 23]

Diagnostic Imaging

Radiographically, osteosarcomas are destructive, poorly delineated osteolytic, osteosclerotic, or mixed lesions (Fig. 17). There may be minimal or massive tumor bone formation within the tumor proper and invading surrounding tissue (Fig. 18). On MR imaging, the tumor appears heterogeneous and demonstrates intermediate signal on T1-weighted and mixed signal intensity (hyperintense and hypointense zones) on T2-weighted MR images. Osteosarcomas demonstrate heterogeneous enhancement on Gd-DTPA–enhanced T1-weighted MR imaging scans (see Fig. 18*B*).

Osteosarcomas of the head and neck are aggressive tumors that are prone to local recurrence and distant metastasis.[42] Multimodality therapy, including complete surgical excision with adjunct radiation and chemotherapy, offers the best chance to control disease as compared with surgery alone.[42] Craniofacial osteosarcomas are associated with a better prognosis than extrafacial tumors.[4, 23] This has been attributed to their tendency to remain localized with metastatic spread only late in the disease course, and a lower histologic grade. In spite of the overall better prognosis of craniofacial osteosarcomas, these are still lethal tumors requiring radical management. The overall 5-year survival rate is no better than 35%.[4, 11, 23] Osteosarcomas arising in Paget's disease are highly malignant with negligible 5-year survival rates.

CHONDROMA

Chondromas of the paraorbital region, including the sinonasal tract and nasopharynx, are rare. The most frequent sites of occurrence include the nasal cavity (septum); ethmoid sinus; and the nasopharynx.[21, 37] There is equal gender predilection and most patients are less than 50 years of age.[12, 37] Symptomatic patients may present with nasal obstruction, enlarging painless mass, proptosis, and headaches.

Sinus opacification or a circumscribed radiolucent lesion can be seen by radiographic studies. Craniofacial chondromas may appear as a polypoid, firm, smooth-surfaced nodule measuring from 0.5 to 2 cm and rarely greater than 3 cm. Histologically, these are lobulated tumors composed of chondrocytes recapitulating the normal histology of cartilage (Fig. 19). Cellular pleomorphism, binucleate chondrocytes, or increased mitotic activity are not present. Craniofacial chondromas should be viewed with some suspicion. Chaudhry et al[12] found that approximately 20% of craniofacial chondrosarcomas are initially misdiagnosed as chondromas.

The differentiation of a chondroma from a well-differentiated chondrosarcoma may at times be difficult if not impossible. For this reason, conservative but complete surgical excision of all craniofacial chondrogenic tumors is the treatment of

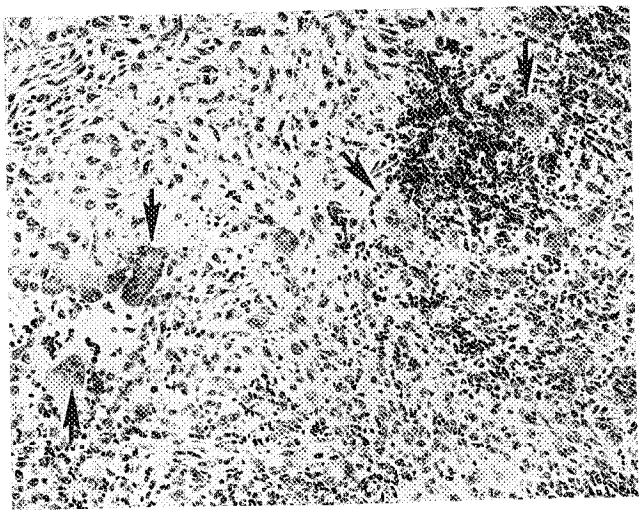

Figure 13. In the giant cell reparative granulomas, the giant cells *(arrows)* are distributed unevenly, with a tendency to cluster in and around foci of hemorrhage *(upper right)* or near vascular spaces *(left)*. An associated cellular fibroblastic stroma is present.

choice. Recurrences of chondromas are uncommon. Tumor recurrence may be indicative of a very well-differentiated chondrosarcoma missed earlier at the time of first diagnosis.

CHONDROBLASTOMA

Chondroblastoma is a benign cartilaginous neoplasm predominantly composed of immature chondrocytes (chondroblasts). Chondroblastomas are uncommon, representing less than 1% of osseous neoplasms.[13] Less than 2% of chondroblastomas occur in the head and neck region.[32] The most common head and neck site of involvement is the temporal bone; less often, chondroblastomas occur in other sites, including craniofacial bones.

Histologically, chondroblastoma are hypercellular tumors composed of mononuclear cells (chondroblasts); randomly distributed multinucleated giant cells; chondroid areas; and calcification taking the form of so-called *chicken wire* or *lacelike pattern* (Fig. 20). The chondroblastic component consists of epithelioid cells with variable-sized round-to-oval nuclei, vesicular-to-hyperchromatic chromatin, and distinct-to-indistinct cell borders.

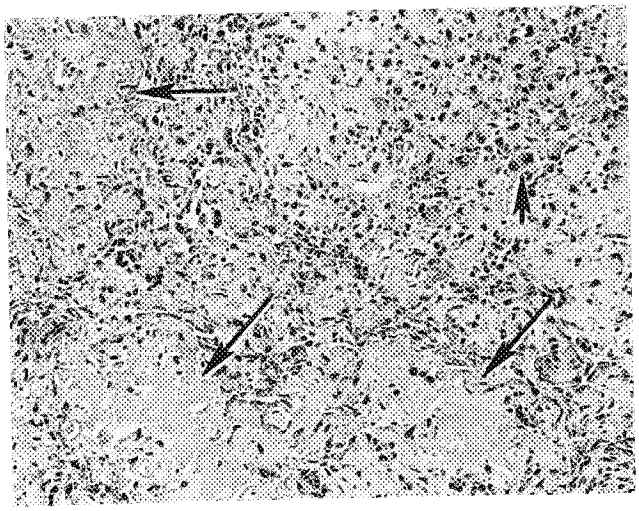

Figure 14. Osteoblastomas are hypercellular with haphazardly arranged trabeculae of osteoid *(large arrows)* associated with a loose fibrovascular connective tissue. Scattered multinucleated giant cells are present *(small arrow)*.

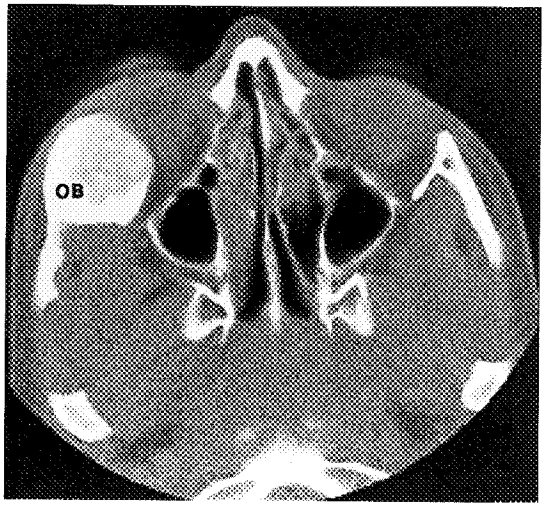

Figure 15. CT scan shows an osteoblastoma (OB) involving the lateral wall of the right orbit.

The nuclei may have indentions, grooves of invaginations creating a bilobed appearance. Spindle-shaped chondroblasts can be seen admixed with the more typical epithelioid chondroblasts. Mitotic figures are present but generally are limited in number and without atypical forms. The chondroid matrix in chondroblastoma is usually limited in extent scattered randomly through the lesion, and appears pink to pinkish blue rather than the typical basophilic appearance of cartilage.[38]

Curettage with or without bone grafting is the treatment of choice and is curative in greater than 90% of cases. Local tumor recurrence occurs within 3 years of surgery and is successfully treated by the repeat curettage or resection. Although Huvos and Marcove[32] found the presence of a coexisting aneurysmal bone cyst component in chondroblastomas to impact adversely on tumor recurrence, Bloem and Mulder[7] found no such correlation. Aggressive behavior in the form of local invasion or distant metastasis (so-called *metastasizing chondroblastomas*) may rarely occur.[32, 35, 39, 51, 56] Treatment for these lesions should include complete resection. Radiotherapy may be used selectively in patients whose tumors are not amenable to surgical resection due to large size or occurrence in surgically inaccessible areas. Rarely, postradiotherapy sarcomas may occur.

CHONDROSARCOMA

The incidence of chondrosarcoma of head and neck sites varies from 5% to 12%.[9, 11, 53] In the head and neck, chondrosarcomas are slightly more common in men than in women and primarily occur in the fourth to seventh decades of life. Approximately 2% of chondrosarcomas occur in patients less than 20 years of age.[9, 11, 33, 43, 53] The most common site of occurrence in the head and neck is the larynx; however, chondrosarcomas occur in virtually all other sites in which cartilage is found but primarily occur in the craniofacial area, including the mandible; maxilla; and maxillofacial skeleton (nose and paranasal sinuses); as well as base of the skull and the nasopharynx.[9, 19, 43, 53, 64] Symptoms vary according to the site of origin. Craniofacial

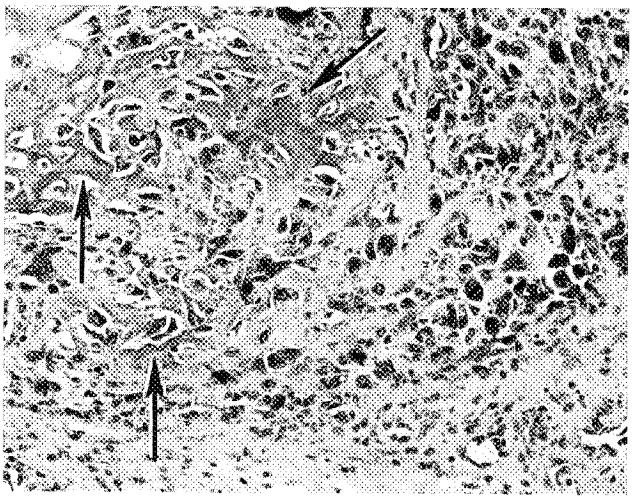

Figure 16. The histopathologic features of osteosarcoma include a sarcomatous stroma intimately admixed and giving rise to osteoid. The latter represents the calcified precursor of bone, appears as eosinophilic, hyalinlike material with irregular contours, and is surrounded by a rim of osteoblasts *(arrows)*. The stromal cells are pleomorphic with hyperchromatic nuclei and increased mitotic activity.

chondrosarcomas may cause nasal obstruction; epistaxis; changes in dentition (loosening or eruption of teeth); proptosis; visual disturbances; and an expanding mass associated with pain, trismus, headaches, and neural deficits.

The radiologic appearance of craniofacial chondrosarcomas is that of a destructive lesion with single or multiple radiolucent, radiopaque, or mixed-appearing areas, and coarse calcifications. The radiographic appearance may correlate with histologic grade.[52] Low-grade chondrosarcomas are uniformly calcified and there is a well-defined demarcation between the tumor and the nonneoplastic bone. In high-grade chondrosarcomas, there are larger portions of the tumor that are not calcified, the calcification that is present tends to be faint and amorphous, and the tumor has an irregular growth and is not well-defined from the nonneoplastic host bone.

The gross appearance of chondrosarcoma includes a smooth, lobulated, hard submucosal mass larger than 2 cm in diameter. Histologically, chondrosarcomas are lobulated, hypercellular tumors

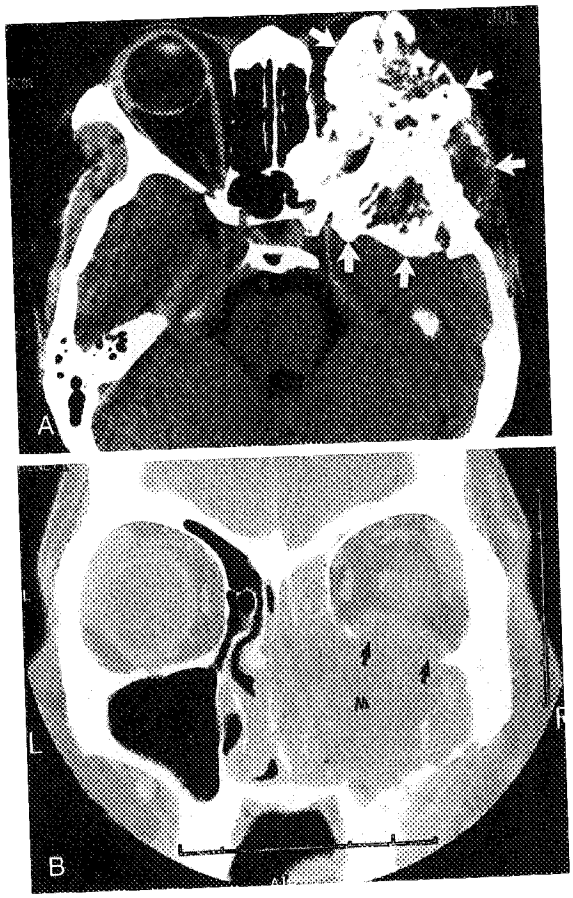

Figure 17. *A*, CT scan shows destructive mass *(arrows)* with marked intratumoral bone formation compatible with osteosarcoma. *B*, CT scan in another patient with chondrogenic osteosarcoma shows destructive mass (M) invading the floor of the orbit *(arrows)*.

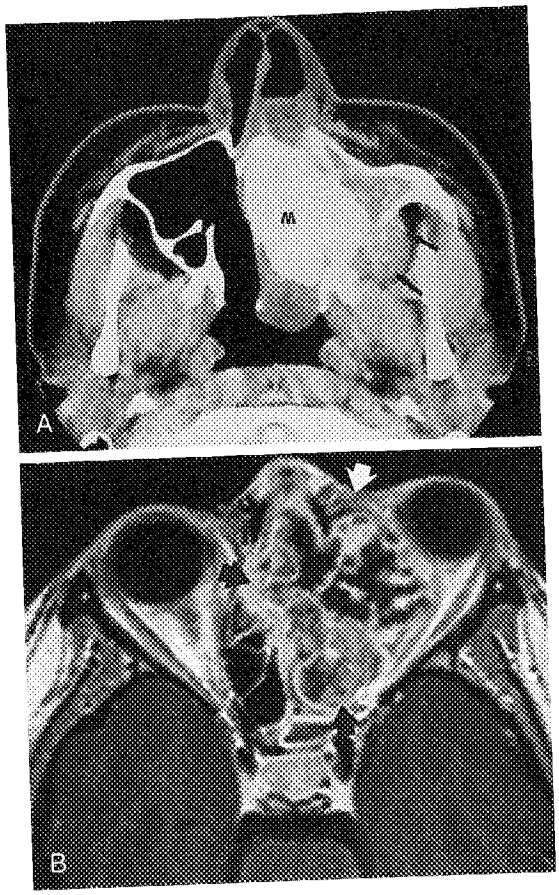

Figure 18. *A*, CT scan shows destructive mass (M) with marked intratumoral bone formation. Note tumor bone formation in the soft tissue component in the infratemporal fossa *(arrows)*. *B*, Enhanced T1-weighted MR image shows heterogeneous contrast enhancement of osteosarcoma *(arrows)*.

composed of cells with hyperchromatic, pleomorphic nuclei; are binucleated or multinucleated; have prominent nucleoli; and have increased mitotic activity (Fig. 21). These cytologic features are used in the histologic grading of chondrosarcomas into three grades. Grade 1, or low-grade chondrosarcomas, have a lobulated appearance with increased cellularity (as compared with a chondroma); enlarged hyperchromatic nuclei; binucleated and, less often, multinucleated cells; limited if any mitosis; and a predominantly chondroid matrix. Necrosis is generally not present. Grade 2, or intermediate-grade chondrosarcomas, have less matrix and increased cellularity as compared with grade 1 tumors. As compared with grade I chondrosarcomas, grade 2 tumors have a lobulated growth; increased cellularity especially toward the periphery of the lobules; greater degree of cellular pleomorphism; more binucleated and multinucleated cells; increased mitotic activity; less of a chondroid matrix with more myxoid stroma; and necrosis (focal to confluent foci). Grade 3 or

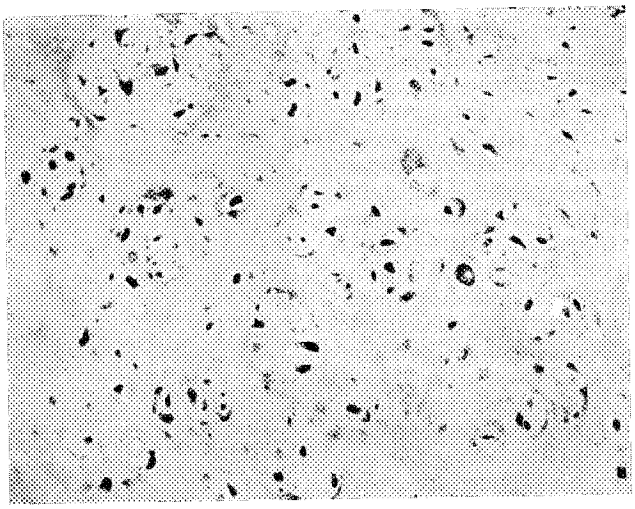

Figure 19. Chondromas are composed of chondrocytes that recapitulate the normal histology of cartilage-lacking, cellular pleomorphism, binucleate chondrocytes or increased mitotic activity.

high-grade chondrosarcomas also tend to be lobulated in appearance but show marked increase in cellularity with greater nuclear pleomorphism, higher mitotic rate, and sparse-to-absent chondroid matrix. Necrosis is a frequent finding often appearing as rather large, confluent areas. It should be noted that any given chondrosarcoma may have an admixture of different histologic grades within the same neoplasm. In this setting, one grade may predominate, with limited foci composed of a different grade. There are no fixed rules governing the grading of these tumors but the diagnosis should be predicated on the dominant histologic grade with an indication that foci of other histologic grade(s), especially higher-grades, are also seen. Histologic variants of chondrosarcoma, including dedifferentiated chondrosarcoma, mesenchymal chondrosarcoma, and clear cell chondrosarcoma, are rare in the sinonasal tract and nasopharynx.

Diagnostic Imaging

Chondrosarcomas may be seen as a nondestructive, fairly well-delineated or destructive, and poorly delineated osteolytic or mixed lesion (Fig. 22). On MR imaging they appear hyperintense on

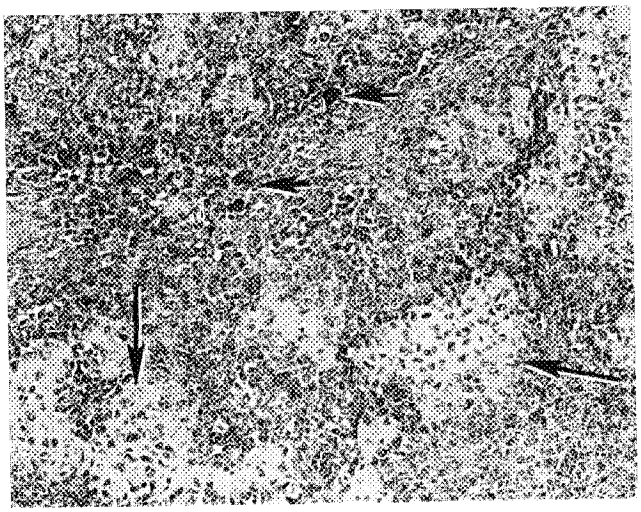

Figure 20. Chondroblastomas are hypercellular tumors composed of mononuclear cells (chondroblasts), scattered multinucleated giant cells *(small arrows)*, chondroid areas *(large arrows)*, and calcification with a lacelike pattern.

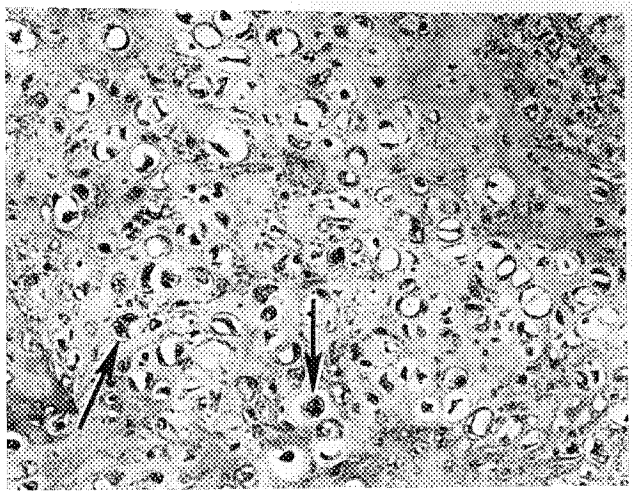

Figure 21. This tumor shows increased cellularity (as compared with a chondroma), enlarged hyperchromatic nuclei, binucleated cells *(arrows)*, and a chondroid stroma.

T1-weighted MR images and moderate-to-marked hyperintense on T2-weighted MR images (Fig. 22). There may be moderate-to-significant enhancement on Gd-DTPA–enhanced T1-weighted MR imaging scans.

For maxillofacial chondrosarcomas, radical resection with adequate margins is indicated.[19] In these sites, chondrosarcoma is a slow-growing but persistent tumor characterized by multiple recurrences. Maxillofacial chondrosarcomas are more le-

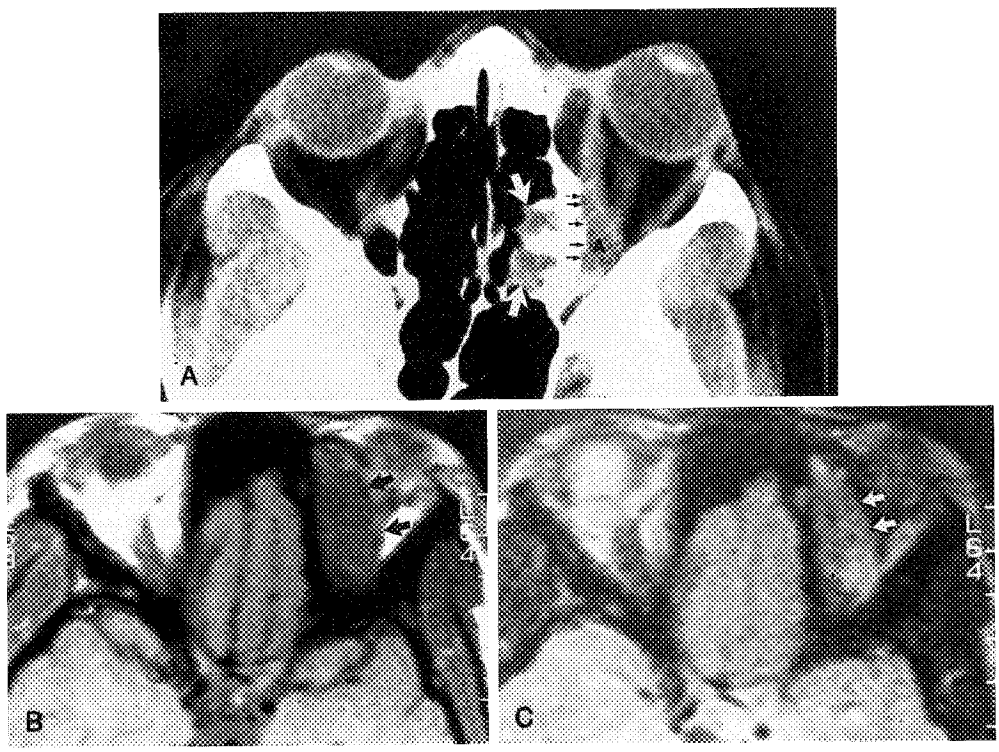

Figure 22. *A*, CT scan shows an ill-defined mass *(white arrows)* involving posterior, ethmoid-air cells. Note sclerosis of the medial orbital wall *(black arrows)* and soft tissue infiltration into the orbital apex. Proton-weighted *(B)* and T2-weighted *(C)* MR image showing orbital component of chondrosarcoma *(arrows)*.

thal than laryngeal chondrosarcoma, perhaps due to their tendency to be of a histologically higher grade[19] but more likely due to their proximity to vital structures and the difficulty in achieving negative margins. Death is generally related to local uncontrolled disease with invasion and destruction of vital structures, including intracranial extension. Neuroaxial or base of skull chondrosarcomas often are extensively infiltrative at the time of diagnosis precluding the ability to completely resect the tumor. Subtotal resection often is the only possible surgical management. As such, chondrosarcomas of the skull base have a tendency to local recurrence. Radiotherapy can be used as an adjunct to surgery as part of the primary management of patients with chondrosarcoma or as adjunctive therapy.[43] The overall 5-year survival rate for head and neck chondrosarcoma is approximately 70%.[9, 43]

CONCLUSION

Fibro-osseous, osseous, and cartilaginous lesions of the orbital and paraorbital regions share overlapping clinical, radiologic, and pathologic features that may lead to diagnostic confusion and possible misdiagnosis. The value of combined clinical-radiologic-pathologic correlation in the diagnosis of fibro-osseous, osseous, and cartilaginous lesions is paramount to achieving the correct diagnosis with subsequent implementation of appropriate therapeutic intervention.

References

1. Albright F, Butler AM, Hampton AO, et al: Syndrome characterized by osteitis fibrosa disseminata, areas of pigmentation and endocrine dysfunction with precocious puberty in females. N Engl J Med 216:727, 1937
2. Anderson DE, McClendon JL: Cherubism-hereditary fibrous dysplasia of the jaws: Genetic considerations. Oral Surg 15:5, 1962
3. Atallah N, Jay MM: Osteomas of the paranasal sinuses. J Laryngol Otol 95:291, 1981
4. Batsakis JG: Osteogenic and chondrogenic sarcomas of jaws. Ann Otol Rhinol Laryngol 96:474, 1987
5. Benedict WF, Fung YK, Murphree AL: The gene responsible for the development of retinoblastoma and osteosarcoma. Cancer 62:1691, 1988
6. Bertoni F, Unni KK, Beabout JW, et al: Giant cell tumor of the skull. Cancer 70:1124, 1992
7. Bloem JL, Mulder JD: Chondroblastoma: A clinical and radiological study of 104 cases. Skeletal Radiol 14:1, 1985
8. Bulow S, Sondergaard JO, Witt I, et al: Mandibular osteomas in familial polyposis coli. Dis Col Rectum 27:105, 1984
9. Burkey BB, Hoffman HT, Baker SR, et al: Chondrosarcoma of the head and neck. Laryngoscope 100:1301, 1990
10. Burland JG: Cherubism: Familial bilateral osseous dysplasia of the jaws. Oral Surg 15:43, 1962
11. Caron AS, Hajdu SI, Strong EW: Osteogenic sarcoma of the facial and cranial bones: A review of forty-three 17 cases. Am J Surg 122:719, 1971
12. Chaudhry AP, Robinovitch MR, Mitchell DR, et al: Chondrogenic tumors of the jaws. Am J Surg 102:403, 1961
13. Dahlin DC, Unni KK: Bone Tumors: General Aspect and Data on 8,542 Cases, ed 4. Springfield, IL, Charles C Thomas, 1986
14. Draper GJ, Sanders BM, Kingston JE: Second primary neoplasms in patients with retinoblastoma. Br J Cancer 53:661, 1986
15. Earwaker J: Paranasal sinus osteomas: A review of 46 cases. Skeletal Radiol 22:417, 1993
16. Emley EW: Giant cell tumor of the sphenoid bone: A case report and review of the literature. Arch Otolaryngol 94:369, 1971
17. Fechner RE, Mills SE: Conventional intramedullary osteosarcoma. *In* Rasai J, Sobin LH (eds): Tumors of the Bones and Joints. Fascicle 8. Third Series. Washington, DC, Armed Forces Institute of Pathology, 1993
18. Fechner RE, Mills SE: Giant cell lesions. *In* Rosai J, Sobin LH (eds): Tumors of the Bones and Joints. Fascicle 8. Third Series. Washington, DC, Armed Forces Institute of Pathology, 1993
19. Finn DG, Goepfert H, Batsakis JG: Chondrosarcoma of the head and neck. Laryngoscope 94:1539, 1984
20. Fu YS, Perzin KH: Non-epithelial tumors of the nasal cavity, paranasal sinuses, and nasopharynx: A clinicopathologic study. II. Osseous and fibro-osseous lesions, including osteoma, fibrous dysplasia, ossifying fibroma, osteoblastoma, giant cell tumor and osteosarcoma. Cancer 33:1289, 1974
21. Fu YS, Perzin KH: Non-epithelial tumors of the nasal cavity, paranasal sinuses, and nasopharynx: A clinicopathologic study. III. Cartilaginous tumor (chondroma, chondrosarcoma). Cancer 34:453, 1974
22. Fullmer HM: Connective tissue components of the periodontium. *In* Milas AEW et al (eds): Chemical and Structural Organization of Teeth. New York, Academic Press, 1967
23. Garrington GE, Scofield HH, Coryn J, et al: Osteosarcoma of the jaws: An analysis of 56 cases. Cancer 20:377, 1967
24. Gibson MJ, Middlemiss JH: Fibrous dysplasia of bone. Br J Radiol 44:1, 1971
25. Gitelis S, Schajowicz F: Osteoid osteoma and osteoblastoma. Orthop Clin North Am 20:313, 1989
26. Glass AG, Fraumeni JF Jr: Epidemiology of bone cancer in children. J Natl Cancer Inst 44:187, 1970
27. Harris WH, Dudley HR Jr, Barry RJ: The natural history of fibrous dysplasia: An orthopedic, pathological and roentenographic study. J Bone Joint Surg 44:207, 1962
28. Harwood AR, Fornasier VL, Rider WD: Supervoltage irradiation in the management of giant cell tumor of bone. Radiology 125:223, 1977
29. Henry A: Monoostotic fibrous dysplasia. J Bone Joint Surg Br 51:300, 1969
30. Hirsch IS, Katz A: Giant cell reparative granuloma outside the jaw bone. Hum Pathol 5:171, 1974
31. Huvos AG, Butler A, Bretsky SS: Osteogenic sarcoma associated with Paget's disease of bone: A clinicopathologic study of 65 patients. Cancer 52:1489, 1983
32. Huvos AG, Marcove RC: Chondroblastoma of bone: A critical review. Clin Orthop 95:300, 1973
33. Huvos AG, Marcove AC: Chondrosarcoma in the young: A clinicopathologic analysis of 79 patients younger than 21 years of age. Am J Surg Pathol 11:930, 1987

34. Huvos AG, Woodard HQ, Cahan WG, et al: Postirradiation osteogenic sarcoma of bone and soft tissues: A clinicopathologic study of 66 patients. Cancer 55:1244, 1985
35. Jambhekar NA, Desai PB, Chitale DA, et al: Benign metastasizing chondroblastoma: A case report. Cancer 82:675, 1998
36. Johnson LC, Youssefi M, Vinh TN, et al: Juvenile active ossifying fibroma: Its nature, dynamics and origin. Acta Otolaryngol Suppl 488:1, 1991
37. Kilby D, Amegaokar AG: The nasal chondroma: Two case reports and a survey of the literature. J Laryngol Otol 91:415, 1977
38. Kurt AM, Unni KK, Sim FH, et al: Chondroblastoma of bone. Hum Pathol 20:965, 1989
39. Kyriakos M, Land VJ, Penning HL, et al: Metastatic chondroblastoma: Report of a fatal case with a review of the literature on atypical, aggressive, and malignant chondroblastoma. Cancer 55:1770, 1985
40. Litter BO: Central giant-cell granuloma of the jaw: A hormonal influence. Br J Oral Surg 17:43, 1979
41. Marcove RC, Weis LD, Vaghaiwalla MR, et al: Cryosurgery in the treatment of giant cell tumors of bone: A report of 52 consecutive cases. Cancer 41:957, 1978
42. Mark RJ, Sercarz JA, Tran L, et al: Osteogenic sarcoma of the head and neck: The UCLA experience. Arch Otolaryngol Head Neck Surg 117:761, 1991
43. Mark RJ, Tran LM, Sercarz J, et al: Chondrosarcoma of the head and neck: The UCLA experience, 1955–1998. Am J Clin Oncol 16:232, 1993
44. Marsh BW, Bonfoglio M, Brady LP, et al: Benign osteoblastoma: Range of manifestations. J Bone Joint Surg 57:1, 1975
45. McCune DJ, Bruch H: Osteodystrophia fibrosa: Report of a case in which the condition was combined with precocious puberty, pathologic pigmentation of the skin and hyperthyroidism, with a review of the literature. Am J Dis Child 54:806, 1937
46. McGowan DA: Central giant cell tumours of the mandible in pregnancy. Br J Oral Med 7:131, 1969
47. Merkow RL, Bansal M, Inglis AE: Giant cell reparative granuloma in the hand: Report of three cases and review of the literature. J Hand Surg 10:733, 1985
48. Nevelle BW, Albenesius RJ: The prevalence of benign fibro-osseous lesions of the peridontal ligament origin in black women: A radiographic survey. Oral Surg 62:340, 1986
49. Oda Y, Tsuneyoshi M, Shinohara N: "Solid" variant of aneurysmal bone cyst (extragnathic giant cell reparative granuloma) in axial skeleton and long bones: A study of its morphologic spectrum and distinction from allied bone lesions. Cancer 70:2642, 1993
50. Resnick D, Niwayama G: Diagnosis of Bone and Joint Diseases, vol 2. Philadelphia, WB Saunders, 1981
51. Reyes CV, Kathuria S: Recurrent and aggressive chondroblastoma of the pelvis with late malignant neoplastic changes. Am J Surg Pathol 3:449, 1979
52. Rosenthal DI, Schiller AL, Mankin HJ: Chondrosarcoma: Correlation of radiological and histological grade. Radiology 150:21, 1984
53. Ruark DS, Schlehaider UK, Shah JP: Chondrosarcomas of the head and neck. World J Surg 16:1010, 1992
54. Saleh EA, Taibh AK, Naguib M, et al: Giant cell tumor of the lateral skull: A case report. Otolaryngol Head Neck Surg 111:314, 1994
55. Seider MJ, Rich TA, Ayala AG, et al: Giant cell tumor of bone: Treatment with radiation therapy. Radiology 161:537, 1986
56. Sirsat MV, Doctor VM: Benign chondroblastoma of bone: Report of a case of malignant transformation. J Bone Joint Surg 52:741, 1970
57. Smith GA, Ward PH: Giant cell lesions of the facial skeleton. Arch Otolaryngol 7:366, 1978
58. Steiner GC, Ghosh L, Dorfman HD: Ultrastructure of giant cell tumors of bone. Hum Pathol 3:569, 1972
59. Taconis WK: Osteosarcoma in fibrous dysplasia. Skeletal Radiol 17:1047, 1988
60. Unni KK, Dahlin DC: Premalignant tumors and conditions of bone. Am J Surg Pathol 3:47, 1979
61. Waldron CA: Osteosarcoma. *In* Neville BD, Damm DD, Allen CM, Bouquot JE (eds): Oral and Maxillofacial Pathology. Philadelphia, WB Saunders, 1985
62. Waldron CA, Giansati JS: Benign fibro-osseous lesions of the jaws: A clinico-pathologic-histologic review of sixty-five cases. II. Benign fibro-osseous lesions of peridontal ligament origin. Oral Surg 35:340, 1973
63. Waldron CA, Shafer WG: The central giant cell reparative granuloma of the jaws: An analysis of 38 cases. Am J Clin Pathol 45:437, 1966
64. Webber PA, Hussain SS, Radcliffe GJ: Cartilaginous neoplasms of the head and neck. J Laryngol Otol 100:615, 1986
65. Wenig BM, Vinh TN, Smirniotopoulos JG, et al: Aggressive psammomatoid ossifying fibromas of the sinonasal region: A clinicopathologic study of a distinct group of fibro-osseous lesions. Cancer 76:1155, 1995
66. Wick MR, Siegel GP, Unni KK, et al: Sarcomas of bone complicating osteitis deformans (Paget's disease): Fifty years' experience. Am J Surg Pathol 5:47, 1981
67. Yabut SM Jr, Kenan S, Sissons HA, et al: Malignant transformation of fibrous dysplasia: A case report and review of the literature. Clin Orthop 228:281, 1988

Address reprint requests to

Mahmood F. Mafee, MD
Department of Radiology
The University of Illinois at Chicago
1740 West Taylor Street
Chicago, IL 60612–7233